

# PATENT COOPERATION TREATY

From the  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

## PCT

To:

WITTE Hubert  
Grenzacherstrasse 124  
CH-4070 Basle  
SUISSE

### NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(PCT Rule 71.1)

Date of mailing  
(day/month/year)

08.03.2006

Applicant's or agent's file reference  
Case 22518

#### IMPORTANT NOTIFICATION

International application No.  
PCT/EP2005/003265

International filing date (day/month/year)  
29.03.2005

Priority date (day/month/year)  
30.03.2004

Applicant  
F. HOFFMANN-LA ROCHE AG et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary report on patentability and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

#### 4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary report on patentability. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed inventions is patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

Name and mailing address of the international  
preliminary examining authority:



European Patent Office - P.B. 5818 Patentlaan 2  
NL-2280 HV Rijswijk - Pays Bas  
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# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference Case 22518	<b>FOR FURTHER ACTION</b> See Form PCT/PEA/416	
International application No. PCT/EP2005/003265	International filing date (day/month/year) 29.03.2005	Priority date (day/month/year) 30.03.2004
International Patent Classification (IPC) or national classification and IPC C12Q1/68, G01N33/50		
Applicant F. HOFFMANN-LA ROCHE AG et al.		
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 8 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> sent to the applicant and to the International Bureau) a total of sheets, as follows:</p> <p style="margin-left: 40px;"><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p style="margin-left: 40px;"><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>		
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the opinion</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input checked="" type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input type="checkbox"/> Box No. VIII Certain observations on the international application</p>		
Date of submission of the demand  06.10.2005	Date of completion of this report  08.03.2006	
Name and mailing address of the international preliminary examining authority:   European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized Officer  Gabriels, J  Telephone No. +31 70 340- 	

**INTERNATIONAL PRELIMINARY REPORT  
ON PATENTABILITY**

International application No.  
PCT/EP2005/003265

**Box No. I Basis of the report**

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
  - ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
    - ☐ international search (under Rules 12.3 and 23.1(b))
    - ☐ publication of the international application (under Rule 12.4)
    - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements\*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report):*

**Description, Pages**

1-16 as originally filed

**Claims, Numbers**

1-18 as originally filed

**Drawings, Sheets**

1/1 as originally filed

☒ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
  - ☐ the description, pages
  - ☐ the claims, Nos.
  - ☐ the drawings, sheets/figs
  - ☐ the sequence listing (*specify*):
  - ☐ any table(s) related to sequence listing (*specify*):
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
  - ☐ the description, pages
  - ☐ the claims, Nos.
  - ☐ the drawings, sheets/figs
  - ☐ the sequence listing (*specify*):
  - ☐ any table(s) related to sequence listing (*specify*):

\* If item 4 applies, some or all of these sheets may be marked "superseded."

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**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

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1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,  
☒ claims Nos. 10,11,18,19 (all completely) 6,7,14,15 (all partially)

because:

- ☒ the said international application, or the said claims Nos. 6,7,14,15 with respect to IA relate to the following subject matter which does not require an international preliminary examination (specify):

**see separate sheet**

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☒ no international search report has been established for the said claims Nos. 10,11,18,19 (all completely)
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
- |                            |  |
|----------------------------|--|
| the written form           | <input type="checkbox"/> has not been furnished            |
|                            | <input type="checkbox"/> does not comply with the standard |
| the computer readable form | <input type="checkbox"/> has not been furnished            |
|                            | <input type="checkbox"/> does not comply with the standard |
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.
- ☐ See separate sheet for further details

**INTERNATIONAL PRELIMINARY REPORT  
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**Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

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1. Statement

Novelty (N)	Yes: Claims	1-9,12-17,20-22
	No: Claims	
Inventive step (IS)	Yes: Claims	
	No: Claims	1-9,12-17,20-22
Industrial applicability (IA)	Yes: Claims	1-5,8,9,12,13,16,17,20-22
	No: Claims	

2. Citations and explanations (Rule 70.7):

**see separate sheet**

**INTERNATIONAL PRELIMINARY REPORT  
ON PATENTABILITY**International application No.  
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**Supplemental Box relating to Sequence Listing**

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**Continuation of Box I, item 2:**

1. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this report has been established on the basis of:
  - a. type of material:
    - ☒ a sequence listing
    - ☐ table(s) related to the sequence listing
  - b. format of material:
    - ☒ in written format
    - ☒ in computer readable form
  - c. time of filing/furnishing:
    - ☒ contained in the international application as filed
    - ☒ filed together with the international application in computer readable form
    - ☐ furnished subsequently to this Authority for the purposes of search and/or examination
    - ☐ received by this Authority as an amendment on
2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional observations, if necessary:

**III. Non-establishment of opinion (Continuation)**

Claims 10,11,18, and 19 have not been searched and claims 6, 7, 14, and 15 have been searched partially. The applicant is reminded that claims or parts thereof for which no International Search Report has been established, will not be the subject of the International Preliminary Examination (Rules 66 (1) (e); 70 (2) (d) PCT).

Claims 6, 7, 14, and 15 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

**V. Reasoned statement (Continuation)**

**1. CITATIONS**

Reference is made to the following documents:

- D1: HOLNESS M J ET AL: "Regulation of pyruvate dehydrogenase complex activity by reversible phosphorylation." BIOCHEMICAL SOCIETY TRANSACTIONS, vol. 31, no. 6, December 2003 (2003-12), pages 1143-1151, XP002337019 ISSN: 0300-5127
- D2: HUANG BOLI ET AL: "Regulation of pyruvate dehydrogenase kinase expression by peroxisome proliferator-activated receptor-alpha ligands, glucocorticoids, and insulin" DIABETES, vol. 51, no. 2, February 2002 (2002-02), pages 276-283, XP002337020 ISSN: 0012-1797
- D3: DATABASE BIOSIS [Online] BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 7 March 2001 (2001-03-07), DONG JIANCHUN ET AL: "Unique properties of human pyruvate dehydrogenase kinase isoform 4 (PDK4)" XP002337025 Database accession no. PREV200100245200
- D4: WU PENGFEI ET AL: "Mechanism responsible for inactivation of skeletal

muscle pyruvate dehydrogenase complex in starvation and diabetes"  
DIABETES, vol. 48, no. 8, August 1999 (1999-08), pages 1593-1599,  
XP002337021 ISSN: 0012-1797

- D5: DATABASE BIOSIS [Online] BIOSCIENCES INFORMATION SERVICE,  
PHILADELPHIA, PA, US; 2003, MINNICK DANA ET AL: "Correlation of change  
in gene expression from skeletal muscle and adipose tissue with efficacy in  
obese rhesus monkeys treated with a PPARpan agonist." XP002337026  
Database accession no. PREV200300459328
- D6: HOLNESS MARK J ET AL: "Up-regulation of pyruvate dehydrogenase kinase  
isoform 4 (PDK4) protein expression in oxidative skeletal muscle does not  
require the obligatory participation of peroxisome-proliferator-activated receptor  
alpha (PPARalpha)" BIOCHEMICAL JOURNAL, vol. 366, no. 3, 15 September  
2002 (2002-09-15), pages 839-846, XP002337022 ISSN: 0264-6021
- D7: WO 2004/027376 A (BRISTOL-MYERS SQUIBB COMPANY; MUKHERJEE,  
RANJAN; LIU, PHILLIP; HUBER,) 1 April 2004 (2004-04-01)

## **2. NOVELTY (Art. 33(2) PCT)**

1. The present application satisfies the criterion set forth in Article 33(2) PCT because the subject-matter of claims 1-9,12-17,20-22 is new in respect of prior art as defined in the regulations (Rule 64(1)-(3) PCT).

## **3. INVENTIVE STEP (Art. 33(3) PCT)**

1. Document D2 is considered to represent the most relevant state of the art and discloses that PDK4 is induced in a tissue-specific manner in response to starvation and diabetes. The findings of D2 suggest that decreased levels of insulin and increased levels of fatty acids and glucocorticoids promote PDK4 gene expression in starvation and diabetes. The subject-matter of claim 1 and 6 differs in that PDK4 expression is used as a biomarker for PPARdelta activity.



2. The problem to be solved by the subject matter of claims 1 and 6 may therefore be regarded as providing a biomarker for PPARdelta activity. The solution would be the expression and/or protein level of PDK4.
3. This solution cannot however be considered as involving an inventive step (Article 33(3) PCT) for the following reasons:
  - (1) The link between PPARalpha and PDK4 was known from the prior art. The relatedness between PPARalpha and PPARdelta would have motivated the person skilled in the art to try PDK4 as a biomarker for PPARdelta activity.
4. The present application does therefore not satisfy the criterion set forth in Article 33(3) PCT and the subject-matter of claims does not involve an inventive step (Rule 65(1)(2) PCT).